```
FILE 'REGISTRY' ENTERED AT 13:48:49 ON 06 SEP 2002

=> S NUCLEASE/CN
L1             1 NUCLEASE/CN

=> D

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   9026-81-7  REGISTRY
CN     ***Nuclease (9CI)***     (CA INDEX NAME)
OTHER NAMES:
CN   Nucleic acid hydrolase
MF   Unspecified
CI   MAN
LC   STN Files:   ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
       CAPLUS, CEN, CHEMCATS, CIN, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB,
       NAPRALERT, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            1720 REFERENCES IN FILE CA (1967 TO DATE)
              44 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            1724 REFERENCES IN FILE CAPLUS (1967 TO DATE)


=> S ENDONUCLEASE/CN
L2             1 ENDONUCLEASE/CN

=> D

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   9055-11-2  REGISTRY
CN   Nuclease, endo- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Cobra venom endonuclease
CN     ***Endonuclease***
MF   Unspecified
CI   MAN
LC   STN Files:   ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
       CAPLUS, CEN, CHEMCATS, CIN, CSCHEM, EMBASE, PROMT, TOXCENTER, USPAT2,
       USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            1339 REFERENCES IN FILE CA (1967 TO DATE)
              15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            1341 REFERENCES IN FILE CAPLUS (1967 TO DATE)

FILE 'CAPLUS' ENTERED AT 13:49:27 ON 06 SEP 2002

=> S NUCLEASE OR ENDONUCLEASE OR L1 OR L2
         18117 NUCLEASE
          5779 NUCLEASES
         22072 NUCLEASE
                 (NUCLEASE OR NUCLEASES)
         22538 ENDONUCLEASE
          7162 ENDONUCLEASES
         26428 ENDONUCLEASE
                 (ENDONUCLEASE OR ENDONUCLEASES)
          1725 L1
          1341 L2
L3       46042 NUCLEASE OR ENDONUCLEASE OR L1 OR L2

=> S METAL
       1357070 METAL
        674823 METALS
L4     1645292 METAL
                 (METAL OR METALS)

=>
=> S EU OR EUROPIUM
         36310 EU
           855 EUS
```

```
        36927 EU
                (EU OR EUS)
        45717 EUROPIUM
            8 EUROPIUMS
        45718 EUROPIUM
                (EUROPIUM OR EUROPIUMS)
L5      63100 EU OR EUROPIUM

=> S L3 AND (L4,L5)
L6        777 L3 AND ((L4 OR L5))

=> S L3 AND L5
L7         47 L3 AND L5

=> D 1-47 TI

=> D 7,8,20,30,36 CBIB ABS
```

L7 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2002 ACS

2001:201752 De novo artificial ***endonucleases*** based on HTH and EF-Hand chimeras. Franklin, Sonya J.; Sirish, Mallena; Welch, Joel T. (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Abstr. Pap. - Am. Chem. Soc., 221st, INOR-601 (English) 2001. CODEN: ACSRAL. ISSN: 0065-7727. Publisher: American Chemical Society.

AB The topol. similarity of helix-turn-helix and EF-hand motifs has been used to design novel lanthanide-binding chimeric peptides with DNA affinity and reactivity. These peptides bind La(III), ***Eu*** (III), and Ca(II), fold in soln. as function of metal, and catalytically hydrolyze model phosphate esters and duplex DNA. The DNA and metal binding properties and cleavage kinetics will be discussed.

L7 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2002 ACS

2001:186104 Document No. 134:363250 De Novo ***Nucleases*** Based on HTH and EF-Hand Chimeras. Welch, Joel T.; Sirish, Mallena; Lindstrom, Katherine M.; Franklin, Sonya J. (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Inorganic Chemistry, 40(9), 1982-1984 (English) 2001. CODEN: INOCAJ. ISSN: 0020-1669. Publisher: American Chemical Society.

AB Small mols. incorporating lanthanide ions have been known since the early 1990s to hydrolytically cleave DNA. However, it remains of great interest to design synthetic ***nucleases*** with the potential to cleave sequences of choice. Artificial enzymes which could target a single promoter region in the genome would have both biochem. utility and pharmaceutical applications as cleavage agents. This has prompted the design of synthetic ***nucleases*** that could exploit the exquisite specificity achieved by DNA binding proteins as a vehicle to deliver a hydrolytic metal to a given sequence for selective cleavage. The present work describes a chimeric motif comprised of a transcription factor DNA-binding domain based on Engrailed and a topol. equiv. Ca-binding EF-hand motif based on calmodulin. The remarkable similarity of the helix orientation in these two unrelated protein turns has been used to design a peptide system with the DNA-binding and metal-binding legacies of the parent structures. The results indicate that these hybrid peptides bind ***Eu*** (III), have metal-dependent structure, and catalyze phosphate hydrolysis of both activated phosphate esters and supercoiled duplex DNA.

L7 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2002 ACS

1996:450927 Document No. 125:108027 Effect of modified nucleotides on structure of yeast tRNAPhe. Comparative studies by metal ion-induced hydrolysis and ***nuclease*** mapping. Michalowski, D.; Wrzesinski, J.; Ciesiolka, J.; Krzyzosiak, W. J. (Inst. Bioorgan. Chem., Polish Acad. Sci., Poznan, 61-704, Pol.). Biochimie, 78(2), 131-138 (English) 1996. CODEN: BICMBE. ISSN: 0300-9084. Publisher: Elsevier.

AB Structural differences between native yeast tRNAPhe, its in vitro transcript and the U8G mutant have been investigated using metal ion-induced hydrolysis and ***nuclease*** digestion. Differences in the soln. structure of the mols. involve four regions: the D- and T-loops, the variable region and the anticodon loop. Efficiency of the Pb(II); ***Eu*** (II)-, Mn(II)- and Mg(II)-induced hydrolysis at the main cleavage sites in the D-loop is significantly reduced for unmodified tRNAs. Moreover, only the in vitro transcripts are susceptible for

cleavage in the T-loop and entire anticodon loop. Other changes in the transcript mol. involve 50-fold enhancement of S1 ***nuclease*** digestion at p36, weak cleavages in the D-loop and lack of some digestion sites in the T-loop. The ***nuclease*** V1 digestion patterns are very similar for studied mols. Changes in the pattern of hydrolysis of the D-loop caused by mutation of the conservative base U8 to G are detected by metal-induced hydrolysis only. Our results indicate clearly that metal ions and enzymic probes monitor different features of RNA structure and their combined use is highly advantageous in studying subtle structural changes in tRNA.

L7 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2002 ACS
1995:26041 Document No. 122:100188 Rare earth metal ions for DNA hydrolysis and their use as artificial ***nuclease*** . Komiyama, Makoto; Takeda, Naoya; Shiiba, Tetsuro; Takahashi, Yota; Matsumoto, Yoichi; Yashiro, Morio (Fac. Engineering, Univ. Tokyo, Tokyo, 113, Japan). Nucleosides & Nucleotides, 13(6-7), 1297-309 (English) 1994. CODEN: NUNUD5. ISSN: 0732-8311.
AB Phosphodiester linkages in linear DNAs are efficiently hydrolyzed by rare earth metal salts. The activities of CeCl3 and Ce(NH4)2(NO3)6 are esp. large. Artificial hydrolytic ***nuclease*** for highly selective scission of DNA has been prepd. by the attachment of Ce(IV) ion to a DNA oligomer as a sequence recognizing moiety.

L7 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2002 ACS
1992:102154 Document No. 116:102154 Efficient catalytic cleavage of RNA by lanthanide(III) macrocyclic complexes: toward synthetic ***nucleases*** for in vivo applications. Morrow, Janet R.; Buttrey, Lisa A.; Shelton, Valerie M.; Berback, Kristin A. (Chem. Dep., State Univ. New York, Buffalo, NY, 14214, USA). J. Am. Chem. Soc., 114(5), 1903-5 (English) 1992. CODEN: JACSAT. ISSN: 0002-7863.
GI

/ Structure 1 in file .gra /

AB Several lanthanide(III) complexes of the hexadentate Schiff base macrocycle (L1; I) were examd. for potential use as RNA transesterification catalysts for in vivo applications. Studies to det. their inertness to metal ion release and ability to cleavage oligomers of RNA were performed. After three days at 37.degree. and pH 7.0, Lu(L1)3+ had completely decompd., Gd(L1)3+ and Tb(L1)3+ had undergone a moderate degree of decompn. (26 and 36%, resp.) and ***Eu*** (L1)3+ and La(L1)3+ had undergone little decompn. (less than 5 and 8% resp.). Only La(L1)3+ and ***Eu*** (L1)3+ were relatively inert at pH 2.5, 37.degree. after 20.5 h. ***Eu*** (L1)3+ was the most resistant to metal release at pH 7.0 in the presence of excess diethylenetriaminepentaacetic acid, with 80% remaining after 20.5 h. Extension cleavage of adenylyl-3',5'-uridine 3'-monophosphate (ApUp) or of oligomers of adenylic acid (A12-A18) was obsd. with 490 .mu.M Ln(L1)3+ or 200 .mu.M Ln(L1)3+ resp. after four hours at neutral pH, 37.degree. (Ln = ***Eu*** , Gd, Tb, La). Pseudo-first-order rate consts. for the cleavage of ApUp by 490 .mu.M ***Eu*** (L1)3+ or for the cleavage of A12-A18 by 160 .mu.M ***Eu*** (L1)3+ were 0.39 h-1 and 1.5 h-1, resp. At pH 7.10 and 37.degree. ***Eu*** (L1)3+ showed catalytic behavior in the transesterification of ApUp; eight turnovers were obsd. with no decrease in reaction rate. Because it efficiently and catalytically cleaves RNA as well as being relatively inert towards metal ion release, ***Eu*** (L1)3+ may find use in in vivo applications of synthetic ***nucleases*** .

=> E FRANKLIN S/AU
=> S E3,E8,E34,E35
5 "FRANKLIN S"/AU
8 "FRANKLIN S J"/AU
23 "FRANKLIN SONYA J"/AU
1 "FRANKLIN SONYA JOAN"/AU
L8 37 ("FRANKLIN S"/AU OR "FRANKLIN S J"/AU OR "FRANKLIN SONYA J"/AU

OR "FRANKLIN SONYA JOAN"/AU)

=> S L8 AND L3
L9 7 L8 AND L3

=> S L8 AND (L4,L5)
L10 19 L8 AND ((L4 OR L5))

=> S L9,L10
L11 21 (L9 OR L10)

=> D 1-21 TI
=> D 1-12,18 CBIB ABS

L11 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2002 ACS
2002:617306 De novo designed helix-hurn-helix metalloproteins. Shields, Sarah B.; ***Franklin, Sonya J.*** (Department of Chemistry, University of Iowa, Iowa City, IA, 52442, USA). Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002, INOR-154. American Chemical Society: Washington, D. C. (English) 2002. CODEN: 69CZPZ.
AB Previous work in our group has focused on chimeric metalloproteins and metallopeptides that were based on the EF-hand ***metal*** binding motifs of calcium binding proteins (e.g. calmodulin) fused with the HTH DNA binding motifs of homeodomain proteins. The success of these designs has led us to a next generation of chimeric proteins. These new designs move beyond the EF-hand motifs to incorporate other physiol. ***metal*** binding sites. The chosen designs have ***metal*** binding residues within a small, contiguous amino acid sequence, as well as having the correct geometry to replace the 90 degree turn of a HTH motif. Expression, ***metal*** binding affinity, and structural characterization of these proteins will be discussed.

L11 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2002 ACS
2002:617304 DNA binding by a new metallopeptide : Transformation of EF-hands to HTH motifs. Kim, Youngbae; ***Franklin, Sonya J.*** (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002, INOR-152. American Chemical Society: Washington, D. C. (English) 2002. CODEN: 69CZPZ.
AB The purpose of this project is to characterize a new group of small ***metal*** -binding peptides that interact with DNA and catalyze hydrolysis of phosphate ester bonds. It is known that the crystal structure of Homeodomains (Helix-turn-helix motif) and Ca-binding proteins (EF-hand motifs) have similar topol., so that the chimeric peptide was designed by combining HTH and EF-hand motifs. The newly designed metallopeptides can interact with DNA since it included a DNA-binding domain. DNA melting temp. studies show that chimeric peptides cause a rise in the m.p., which means the chimeric metallopeptides stabilize double stranded DNA. Agarose gel electrophoresis, binding gel and cleavage gel, have been used to investigate DNA-peptide interaction and cleavage. CD and Fluorescence have been used to det. ***metal*** binding affinity of peptide, and their interaction with DNA. The result will be present in detail.

L11 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2002 ACS
2002:529527 Hydrolytically active ***Eu*** (III) and Ce(IV) EF-hand peptides. Sirish, Mallena; ***Franklin, Sonya J.*** (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Journal of Inorganic Biochemistry, 91(1), 253-258 (English) 2002. CODEN: JIBIDJ. ISSN: 0162-0134. Publisher: Elsevier Science Inc..
AB A chimeric peptide (P4) has been designed to incorporate an EF-hand ***metal*** -binding loop into the context of the helix-turn-helix DNA binding motif of the engrailed homeodomain. This construct binds lanthanides, and in the presence of these ***metals*** , promotes the cleavage of supercoiled DNA and model phosphate esters (bisnitrophenyl phosphate). P4 binds lanthanides with moderate affinities (***Eu*** (III), log Ka=4.85; and Ce(IV), log Ka=5.23). The structure of P4 is enhanced by ***metal*** binding, but the increase in secondary structure obsd. by CD is small, and suggests the metallopeptide is also quite flexible. Despite this flexibility, the efficient cleavage of DNA

at low concns. is dependent on the metallopeptide, and not on peptide or ***metal*** alone. This enhanced reactivity suggests the designed DNA-binding EF-hand peptides deliver the ***metal*** to the DNA for catalysis, even without rigid secondary structure.

L11 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2002 ACS
2001:639317 Highly efficient complexation of lanthanide ions by peptide chimeras based on HTH and EF-hand motifs. Mallena, Sirish; ***Franklin,*** *** Sonya J.*** (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001, INOR-130. American Chemical Society: Washington, D. C. (English) 2001. CODEN: 69BUZP.
AB A new class of peptide chimeras based on HTH and EF-hand motifs of DNA binding protein, engrailed; and calcium binding protein, calmodulin resp. have been designed and synthesized. Fluorescence spectral studies indicate that these peptides display strong affinities towards various Ln(III) as well as Ce(IV) and Ca(II) ***metal*** ions. 1H NMR titrns. carried out on these peptides and the above ***metals*** reveal a ***metal*** dependent structural changes in soln. Investigations on the ***metal*** binding affinities using fluorescence and 1H NMR techniques; as well on the ***metal*** induced binding and cleavage of plasmid DNA by these ***metal*** -peptide chimeras will be discussed.

L11 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2002 ACS
2001:639292 Chimeric helix-turn-helix ***endonuclease*** : DNA-metallopeptide interactions. Kim, Youngbae; ***Franklin, Sonya*** *** J.*** (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001, INOR-105. American Chemical Society: Washington, D. C. (English) 2001. CODEN: 69BUZP.
AB We are designing and characterizing a new group of small metallopeptides as artificial ***endonucleases*** , which act as DNA binding and cleavage agents. Helix-turn-helix (HTH) and EF-hand motifs have been used to design chimeric peptides based on their similar topol. These de novo lanthanide binding peptides comprise EF-hand and HTH motifs, in which the Ca-binding EF-hand motif is inserted into THT motif at the turn. These chimeric peptides (P3, P4, and P5) not only have DNA binding affinity but also catalyze DNA cleavage as long as they retain parental structure and ***metal*** chelating properties. CD, UV, NMR, and fluorescence have been used to det. secondary structure, ***metal*** binding affinities, and DNA cleavage kinetics. Agarose gel electrophoresis and DNA melting temp. studies have been used to investigate DNA-peptide interactions. The results will be presented in detail.

L11 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2002 ACS
2001:639291 DNA cleavage by homeodomain protein chimeras. Kovacic, Roger Timothy; Lim, Sunghyuk; Harris, Kinesha; Rathe, Jennifer; ***Franklin,*** *** Sonya J.*** (Department of Chemistry, The University of Iowa, Iowa City, IA, 52242, USA). Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001, INOR-104. American Chemical Society: Washington, D. C. (English) 2001. CODEN: 69BUZP.
AB De novo design of site-specific ***endonucleases*** could be very useful in targeting and eliminating oncogenes. In order to develop such catalysts we have designed several protein systems based on site-specific DNA binding proteins contg. the helix-turn-helix (HTH) binding motif. Since the EF hand begins and ends with helixes that perfectly match the orientation of the HTH and the motif binds calcium and lanthanides, it is a good candidate for mediating DNA cleavage. We have combined the helixes of several DNA binding proteins with the EF hand by peptide synthesis and protein engineering. Here we report the cloning and characterization of chimeric proteins and progress toward detg. the cutting specificity of these chimeras using std. mapping techniques and Maxam-Gilbert sequencing technol.

L11 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2002 ACS
2001:321723 Document No. 135:72740 Lanthanide-mediated DNA hydrolysis. ***Franklin, Sonya J.*** (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Current Opinion in Chemical Biology, 5(2), 201-208 (English) 2001. CODEN: COCBF4. ISSN: 1367-5931. Publisher: Elsevier Science Ltd..
AB A review, with 48 refs. Lanthanide ions are remarkably effective

catalysts for the hydrolytic cleavage of phosphate ester bonds, including the robust bonds of DNA. This makes Ln(III) and Ce(IV) ions attractive candidates for developing selective and efficient artificial ***nucleases*** , which could have many biochem. and clin. applications. Both small-mol.-based and biopolymer-based lanthanide complexes are being pursued.

L11 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2002 ACS
2001:240886 Document No. 134:367184 Chimeric HTH motifs based on EF-hands. Kim, Youngbae; Welch, Joel T.; Lindstrom, Katherine M.; ***Franklin,*** *** Sonya J.*** (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). JBIC, Journal of Biological Inorganic Chemistry, 6(2), 173-181 (English) 2001. CODEN: JJBCFA. ISSN: 0949-8257. Publisher: Springer-Verlag.

AB The design of a new peptide construct from two structurally equiv. basis motifs is reported. A chimera was designed from the helical regions of a helix-turn-helix (HTH) domain, incorporating the consensus EF-hand Ca-binding loop at the turn. Two 33-residue peptides were constructed: one (P3, designed) includes the 12-residue consensus EF-hand loop, while the other (P2, control) contains the reversed EF-hand loop sequence. The ***Eu*** (III) and Ca(II) binding properties of P2 and P3 were investigated by CD and NMR. The designed peptide (P3) is 25% helical in its ***Eu*** (III)-satd. form, and 14% helical with excess Ca(II). Both the free and ***Eu*** -bound peptides have inherent soln. structure, as demonstrated by the helicity induced by the addn. of trifluoroethanol solvent. While ***Eu*** (III) binding stabilizes the structure of P3, it destabilizes the structure of P2. The NMR titrn. of P3 with ***Eu*** (III) resulted in new resonances characteristic of Ca-bound EF-hand loops. As obsd. for isolated EF-hands, the resonances appear within the first 0.5 equiv of ***Eu*** (III) added, suggesting that one ***metal*** ion organizes two equiv. of peptide to fold into the back-to-back dimer structure of native EF-hands. The EuP3 chimera, but not EuP2, has significant affinity for supercoiled plasmid DNA, causing a gel shift at concns. as low as 10 .mu.M EuP3 (50 .mu.M base pairs). These results show our chimeric peptide combines the characteristics of the parent motifs, maintaining both ***metal*** binding and DNA affinity.

L11 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS
2001:201752 De novo artificial ***endonucleases*** based on HTH and EF-Hand chimeras. ***Franklin, Sonya J.*** ; Sirish, Mallena; Welch, Joel T. (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Abstr. Pap. - Am. Chem. Soc., 221st, INOR-601 (English) 2001. CODEN: ACSRAL. ISSN: 0065-7727. Publisher: American Chemical Society.

AB The topol. similarity of helix-turn-helix and EF-hand motifs has been used to design novel lanthanide-binding chimeric peptides with DNA affinity and reactivity. These peptides bind La(III), ***Eu*** (III), and Ca(II), fold in soln. as function of ***metal*** , and catalytically hydrolyze model phosphate esters and duplex DNA. The DNA and ***metal*** binding properties and cleavage kinetics will be discussed.

L11 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2002 ACS
2001:201213 De novo design of ***metal*** binding peptides as artificial ***endonucleases*** . Sirish, Mallena; ***Franklin, Sonya J.*** (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Abstr. Pap. - Am. Chem. Soc., 221st, INOR-093 (English) 2001. CODEN: ACSRAL. ISSN: 0065-7727. Publisher: American Chemical Society.

AB Here, we describe on the de novo design of a class of chimeric peptides P4 and P4a based on helix-turn-helix and EF-Hand motifs. These peptides bind various ***metals*** including lanthanides and calcium. These peptides exhibit ***metal*** dependent structure, catalyze the hydrolysis of bis-nitrophenylphosphate (BNPP), a model compd. as well as the duplex DNA. The studies on the secondary structure, ***metal*** binding affinities as well as the DNA cleavage kinetics of these ***metal*** -peptide complexes will be presented in detail.

L11 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS
2001:186104 Document No. 134:363250 De Novo ***Nucleases*** Based on HTH and EF-Hand Chimeras. Welch, Joel T.; Sirish, Mallena; Lindstrom, Katherine M.; ***Franklin, Sonya J.*** (Department of Chemistry,

University of Iowa, Iowa City, IA, 52242, USA). Inorganic Chemistry, 40(9), 1982-1984 (English) 2001. CODEN: INOCAJ. ISSN: 0020-1669. Publisher: American Chemical Society.

AB Small mols. incorporating lanthanide ions have been known since the early 1990s to hydrolytically cleave DNA. However, it remains of great interest to design synthetic ***nucleases*** with the potential to cleave sequences of choice. Artificial enzymes which could target a single promoter region in the genome would have both biochem. utility and pharmaceutical applications as cleavage agents. This has prompted the design of synthetic ***nucleases*** that could exploit the exquisite specificity achieved by DNA binding proteins as a vehicle to deliver a hydrolytic ***metal*** to a given sequence for selective cleavage. The present work describes a chimeric motif comprised of a transcription factor DNA-binding domain based on Engrailed and a topol. equiv. Ca-binding EF-hand motif based on calmodulin. The remarkable similarity of the helix orientation in these two unrelated protein turns has been used to design a peptide system with the DNA-binding and ***metal*** -binding legacies of the parent structures. The results indicate that these hybrid peptides bind ***Eu*** (III), have ***metal*** -dependent structure, and catalyze phosphate hydrolysis of both activated phosphate esters and supercoiled duplex DNA.

L11 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS

2000:331267 DNA cleavage by a new motif: Artificial ***endonucleases*** based on the EF-hand.. ***Franklin, Sonya J.*** ; Lindstrom, Katherine M.; Kim, Youngbae (Department of Chemistry, University of Iowa, Iowa City, IA, 52242, USA). Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000, INOR-486. American Chemical Society: Washington, D. C. (English) 2000. CODEN: 69CLAC.

AB The topol. similarity of helix-turn-helix and EF-hand motifs (figure) has been used to design novel chimeric peptides with DNA binding affinity and reactivity. The Ln(III) and Ca(II) binding properties and DNA binding affinities of a series of peptides have been studied. The kinetics of phosphate hydrolysis in duplex NA and model phophate esters will be discussed.

L11 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2002 ACS

1994:714487 Document No. 121:314487 Solution Structure and Dynamics of Lanthanide Complexes of the Macrocyclic Polyamino Carboxylate DTPA-dien. NMR Study and Crystal Structures of the Lanthanum(III) and ***Europium*** (III) Complexes. ***Franklin, Sonya J.*** ; Raymond, Kenneth N. (Department of Chemistry, University of California at Berkeley, Berkeley, CA, 94720, USA). Inorg. Chem., 33(25), 5794-804 (English) 1994. CODEN: INOCAJ. ISSN: 0020-1669.

GI

/ Structure 2 in file .gra /

AB An 18-membered macrocyclic DTPA-bis(amide) ligand (I; DTPA = diethylenetriaminepentaacetic acid) contg. a heteroatom in the amide link was prepd. via the condensation of DTPA-dianhydride and diethylenetriamine. The soln. structures of the two isomeric pairs present in the Ln(III) complexes of DTPA-dien were studied by 1H NMR. One enantiomeric pair exhibits slow exchange on the NMR time scale at low temps. (0-25.degree.) and dynamic behavior at higher temps. The other isomeric pair exhibits an unusual static behavior; exchange remains slow even at 95.degree.. Peak assignments for the ***Eu*** (DTPA-dien) spectra are given based on deuteration studies, 2-dimensional COSY spectroscopy, and 2-dimensional EXSY spectroscopy. 2D EXSY spectroscopy at several temps. and mixing times showed that .DELTA.G.thermod.299 for the dynamic isomerization is 57.5 .+-. 0.3 kJ/mol, and that the dynamic isomer is an intermediate for the static isomerization, which occurs with a change in backbone amine chirality. The structures of the La(III) and ***Eu*** (III) DTPA-dien complexes were detd. by x-ray anal. [La(DTPA-dienH+)H2O]2(CF3SO3-)2.cntdot.18H2O crystallizes as a carboxylate-bridged dimer about a center of inversion in the orthorhombic space group Pbca with a 12.626(2), b 21.405(3), c 26.422(9) .ANG., and Z =

8. Each La ion is 11-coordinate with octadentate ligand coordination, an .eta.2 bridging carboxylate, and one H2O. [***Eu*** (DTPA-dienH+)]4(CF3SO3-)4.cntdot.6NaCF3SO3.cntdot.20H2O crystallizes as a carboxylate-bridged tetramer with two crystallog. independent ***Eu*** (III) positions (Z = 8 for each) in the monoclinic space group C2/c: a 30.94(1), b 23.456(3), c 22.611(4) .ANG., .beta. 105.78(2).degree.. The coordination geometries about Eu1 and Eu2 are nearly identical and are described as a nine-coordinate tricapped trigonal prism with octadentate ligand coordination plus an .eta.1 bridging carboxylate. The tendency to oligomerize is attributed to the constraints imposed by the macrocycle and the H bonding available with the link heteroatom. The structural differences between the two complexes are attributed to a difference in La(III) and ***Eu*** (III) ionic size. The soln. structure of the dynamic isomer is the same as the monomer unit of the crystal structures, and the static isomer is similar, save for a change in one terminal backbone nitrogens' chirality.

	L #	Hits	Search Text	DBs
1	L1	22966	NUCLEASE OR ENDONUCLEASE	USPAT ; US-PG PUB
2	L2	1129475	METAL	USPAT ; US-PG PUB
3	L3	11945	EU OR EUROPIUM	USPAT ; US-PG PUB
4	L4	217	L1 NEAR10 (L2 OR L3)	USPAT ; US-PG PUB